PATENT SPECIFICATION

NO DRAWINGS

Inventor: EUGENE L. LEROI

1,153,640

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Date of filing Complete Specification: 13 May, 1968.

Application Date: 10 April, 1967. No. 16382/67.

Complete Specification Published: 29 May, 1969.

Index at acceptance: —C2 C(LW20Y, LW29Y, LW290, LW30Y, LW32Y, LW36Y, LW362, LW366, LW367, LW620, LW628, LW650, LW79Y, LW790)

Int. Cl: —C 07 c 101/30

ERRATUM

SPECIFICATION NO. 1,153,640

Page 1, for Index at Acceptance C2C only read:-

(20Y, 29Y, 290, 30Y, 32Y, 36Y, 362, 366, 367, 620, 628, 650, 79Y, 790, LW)

THE PATENT OFFICE,
10th December 1969

D 120573/41

OH

and therapeutic compositions whose principal ingredient it is. These new compositions are interesting for they increase the pepsic secretions in a pH range favourable to digestion. They may take any of the usual pharmaceutical forms such as pills, capsules or tablets and the latter may comprise an admixture with an excipient. The usual pharmaceutical excipient such as sugar, starch or talc may be used.

The preparation of monocarnitin citrate may be performed by any of the following processes:

1. From Carnitin hydrochloride and citric acid

Carnitin hydrate is prepared, by treatment of carnitin hydrochloride either with an alkali metal hydroxide or bicarbonate, preferably sodium hydroxide or sodium bicarbonate.

a) Using sodium hydroxide

Caustic soda pellets are dissolved in methyl alcohol and added dropwise to a stoichiometric amount of carnitin hydrochloride dissolved in methyl alcohol. The precipitated sodium chloride is filtered off and to the solution — which contains carnitin hydrate — there is added a stoichiometric amount of citric acid, dissolved in methyl alcohol. The mixture is evaporated and dried. The product is washed with acetone and purified by crystallisation from anhydrous ethyl alcohol.

b) Using sodium bicarbonate

To an aqueous concentrated solution of carnitin hydrochloride is added a stoichiometric amount of sodium bicarbonate. After stirring, a stoichiometric amount of citric acid — dissolved in methyl alcohol — is added, and the sodium chloride precipitated is filtered off. The mixture is evaporated under reduced pressure. The product is precipitated by addition of acetone, filtered and purified as in 1a) above.

2. From carnitin hydrochloride and sodium citrate

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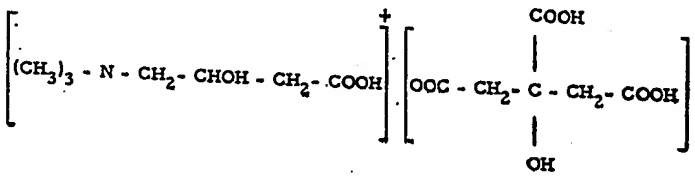
COMPLETE SPECIFICATION

A Carnitin Salt

We, SOCIETE D'ETUDES DE PRODUITS CHIMIQUES, a Societe a responsabilite limitee organised under the laws of France of 16, Rue, Kleber, Issy-les-Moulineaux, Seine, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement: —

The invention relates to monocarnitin citrate of the formula:



and therapeutic compositions whose principal ingredient it is. These new compositions are interesting for they increase the pepsic secretions in a pH range favourable to digestion. They may take any of the usual pharmaceutical forms such as pills, capsules or tablets and the latter may comprise an admixture with an excipient. The usual pharmaceutical excipient such as sugar, starch or talc may be used.

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b) Using sodium bicarbonate

To an aqueous concentrated solution of carnitin hydrochloride is added a stoichiometric amount of sodium bicarbonate. After stirring, a stoichiometric amount of citric acid — dissolved in methyl alcohol — is added, and the sodium chloride precipitated is filtered off. The mixture is evaporated under reduced pressure. The product is precipitated by addition of acetone, filtered and purified as in 1a) above.

2. From carnitin hydrochloride and sodium citrate

SEE ERRATA SLIP ATTACHED

Both compounds, in stoichiometric proportions, are dissolved in the monomethyl ether of ethylene glycol. The solution is boiled to reflux for one hour. Sodium chloride is filtered off, the filtrate is evaporated under reduced pressure and acetone is added for the precipitation of the product. The end of the treatment is as in 1b) above.

3. From carnitin sulphate and barium citrate

To a hydroalcoholic solution of carnitin sulphate, is added a stoichiometric amount of barium citrate. After stirring and filtration of the precipitated barium sulphate, the solution is evaporated under reduced pressure and the treatment is ended as in 2 above.

4. By ion exchange technique

a) From carnitin hydrochloride and sodium citrate

An aqueous solution of carnitin hydrochloride is passed over a Dowex 50 resin (Dowex is a Registered Trade Mark) until saturation in carnitin is reached. The resin is washed and, after determination of the fixed carnitin, an aqueous solution of the stoichiometric amount of sodium citrate is passed over the resin. The soda is fixed on the resin and the solution contains monocarnitin citrate. The solution is evaporated under reduced pressure. The end of the treatment is as in 2 above.

b) From carnitin hydrochloride and citric acid

An aqueous solution of carnitin hydrochloride is passed over an Amberlite IR 45(OH) resin (Amberlite is a Registered Trade Mark). Hydrochloric acid is fixed. The amount of carnitin in solution is determined by analysis. The stoichiometric amount of citric acid added. The end of treatment as in 4a) above.

For methods 1 to 3, the yields are about from 60 to 70%; for method 4, about 80%.

WHAT WE CLAIM IS:—

1. Monocarnitin citrate.

2. A process for the preparation of monocarnitin citrate in which carnitin hydrochloride is treated with an alkali metal hydroxide or bicarbonate and then with citric acid.

3. A process according to Claim 2 in which the hydrochloride is dissolved in methyl alcohol and treated with sodium hydroxide.

4. A process according to Claim 2 in which the hydrochloride is treated in concentrated aqueous solution with sodium bicarbonate and then with citric acid dissolved in methyl alcohol.

5. A process for the preparation of monocarnitin citrate in which carnitin hydrochloride and sodium citrate dissolved in the monomethyl ether or ethylene glycol and boiled under reflux.

6. A process for the preparation of monocarnitin citrate in which carnitin sulphate in hydroalcoholic solution is treated with barium citrate.

7. A process for the preparation of monocarnitin citrate in which an aqueous solution of carnitin hydrochloride is passed over an ion exchange resin so that the carnitin is fixed, an aqueous solution of sodium citrate is passed over the resin and the solution obtained is evaporated under reduced pressure.

8. A process for the preparation of monocarnitin citrate in which an aqueous solution of carnitin hydrochloric is passed over an ion exchange resin so that hydrochloride acid is fixed and citric acid is added to the solution.

9. A process for the preparation of monocarnitin citrate substantially as herein described.

10. Monocarnitin citrate prepared by a process according to any of Claims 2 to 9.

11. A therapetic composition containing monocarnitin citrate in admixture with a pharmaceutical excipient.

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Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa—1969.
Published by The Patent Office, 25 Southampton Buildings, London, W.C.2., from which copies may be obtained.